201-14290A

HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN
FOR
ALDEHYDES, C4, SELF-CONDENSATION PRODUCTS, HIGH-BOILING FRACTION
(CAS NO.: 68990-21-6)

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PREPARED BY:

EASTMAN CHEMICAL COMPANY

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OVERVIEW

The Eastman Chemical Company hereby resubmits for review and public comment the test plan for aldehydes, C4, self-condensation products, high-boiling fraction (Solvent C; CAS NO.: 68990-21-6) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. It is believed that the information within this revised plan addresses many of the concerns raised by the EPA. This new submission provides better documentation and clarity as to the hazard potentials of the data available on the chemicals identified in Solvent C and why such data should be deemed as adequate to make an assessment of the hazards and risk associated with Solvent C.

Solvent C is a by-product produced through the summation of waste streams from four different manufacturing processes. Thus, it is a Class 2 chemical and may consist of many different chemicals with approximately 10 major constituents. These ten major constituents may be present in varying concentration ranging from zero to levels typically found, and listed in Table 1 below. Due to the fact that it is a mixture with a widely varying composition, specific physical chemical properties, as well as some environmental fate assessments cannot be determined or estimated with the current modeling programs. In addition, we believe that this highly varying composition precludes the ability to conduct of any animal studies of meaningful reliability. Such concerns are grounded in the October 14 1999 letter sent by the EPA in which companies are urged to forego animal testing when the relevance of data generated are of uncertain relevance. However, we believe an assessment of the hazard potential for Solvent C can be surmised through the use of data that currently exist on most of the individual chemicals that may be found within Solvent C.

Since there have been no studies specifically conducted on Solvent C, Eastman has tried to address each SIDS endpoint through a brief synopsis of the data available for each of the individual chemicals. Each data synopsis is used to demonstrate and support our conclusion that Solvent C does not pose a significant hazard requiring further study. Much of the data Eastman utilized to draw our conclusions is currently available to the public as a result of previous submissions to the US HPV program, OECD SIDS program, or through their presence in peer-reviewed journal articles and reviews. Data are also available through the US Food and Drug Agency (FDA) on 5 of the 10 major components, as they have been approved under 21 CFR 172.515 for use in foods at low levels. These five chemicals may comprise almost a third of Solvent C on a quantitative basis. Some data utilized in our assessment was obtained from draft reports from ongoing ICCA submissions, and will only be available to the public (in the form of robust summaries) after the EPA has reviewed them to ensure their completeness and quality. In addition, some data have been previously reviewed by the EPA as part of an approval for its use as an insect repellant for human use. Such data were assumed to be of suitable quality; this assumption is fortified by their presence in peer-reviewed journals too. Another chemical present in the mixture not in any formalized review program is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. Such an approved use could result in significant releases into the environment. The EPA website indicates it is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients and it is believed that they will be available to the public. Acute toxicity data indicate this material is classified as relatively harmless (LD_{50} 33,900 mg/kg). In total, these data demonstrate wide margins of safety relative to the potential exposures.

While the HPV program is a hazard identification program, Eastman believes the need to conduct studies, especially when they may be of questionable reliability or involve animals, needs to take into account the type and amounts of exposure that may occur. Briefly, as detailed in the test plan summary, exposure to Solvent C is extremely low as it is handled in essentially closed systems with primary end uses that preclude exposures of any significance. Possible exposures during shipping from its loading and unloading would also occur on an intermittent basis.

In summary, Eastman, through the use of information already generated on the components of Solvent C, has concluded that this chemical mixture is likely of a low hazard potential to both the environment and mammalian systems and is without need for the conduct of any new or additional tests. The information used to make this assessment is contained within this submission and constitutes a fulfillment of our obligation to the HPV program to supply the public with information about the hazard potential and risks associated with this chemical.

TEST PLAN SUMMARY

Solvent C is a yellow-green liquid Class 2 chemical by-product from the combination of the waste streams from four different processes used in the manufacture of other chemicals. It is usually comprised of approximately 10 major chemicals whose presence, and percentage, is dictated by the contributing waste stream. Since each waste stream contributes a different set of components to Solvent C, the presence or absence of any particular waste stream will significantly alter the composition of Solvent C. Thus, the percentage level at which any one constituent may be present can vary from almost 0 to the typical ranges listed in the table below (See Table 1).

Of the 10 major constituents, 7 have already been, or are in the process of being, evaluated through the OECD or ICCA SIDS program, or the US HPV program (neopentyl glycol, 2,2,4-trimethyl-1,3-pentanediol, n-butyl alcohol, 2-ethylhexanol, isobutyl alcohol, isobutyl isobutyrate, and butyric acid). Such reviews will ensure the hazards of each chemical have been adequately characterized.

Of the remaining three major constituents not in any formalized HPV programs, one, butyl butyrate, has been approved by the FDA as a synthetic flavoring agent for food under 21CFR 172.515 and is found naturally in many types of fruits. A European regulatory body has concluded it to have an acceptable daily intake (ADI) of up to 1 mg/kg/day. This compound is formed through an ester linkage between n-butanol and butyric acid. In biological systems, it would be expected that this ester linkage would readily be cleaved to yield the parent molecules butyric acid and butanol; both of these chemicals are also found in Solvent C and are in the ICCA SIDS program. In actuality, the FDA has approved five of the 10 major chemicals in Solvent C for use in foods (butyl butyrate, n-butyl alcohol, isobutyl alcohol, isobutyl isobutyrate, and butyric acid). These five chemicals, in a quantitative manner, make up almost one third of "typical" Solvent C.

Another nonHPV chemical present in Solvent C, 2-ethyl-1,3-hexanediol, was at one time registered with the EPA for use as an insect repellant for use by humans. Such a use dictated the generation of significant amounts of hazard data for EPA review and can now also be found in peer-reviewed journals. Other documentation of its safety can be surmised through its potential use as a solvent in some cosmetic products. The safety of this use was reviewed for the FDA by the Cosmetics Ingredients Review (CIR) Expert Panel with their conclusions (safe as used in concentrations up to 5%) published (J. Amer. Coll. Toxicol 13(6):418-436 1994).

The third nonHPV chemical found in Solvent C, di-2-ethylhexyl ether, has no data beyond an assessment of its acute toxicity available to the public. However, concern over its risks should be somewhat mitigated by the fact that its reported LD_{50} in rats is almost 34 g/kg (Smyth 1954). In addition, no toxicity structural alerts for mutagenicity or carcinogenicity were identified through the use of computer modeling programs (DEREK). Another program predicted this molecule would likely undergo simple oxidative metabolism of the side chains followed by phase II conjugation reactions to allow for its excretion. Further support that the inherent toxicity of this molecule should be considered low is garnered from the fact that the EPA allows for the use of this compound in pesticides as it is listed as a Class 3 inert ingredient on their website. It is assumed the potential exposure to man and the environment from such a use would greatly exceed that from its presence in Solvent C. The EPA's Office of Pesticide Programs has indicated on their website that they have contracted a Structure Activity Team (SAT) to prepare toxicological and ecological assessments for Class 3 inert ingredients. This review will be made available to the public. Should this review indicate this chemical does pose a significant hazard, Eastman will update this current submission with their conclusions and perform a new risk assessment.

Another component of Solvent C is described as being "alkyl acetals". These chemicals are formed by a reaction between alcohols and aldehydes. Such reactions are readily reversed in the presence of an acid. It is unknown how much of a hazard these chemicals may pose, as they have not been qualitatively identified so no data could be located for them. However, they also are a mixture of many different individual compounds and their combined presence only totals 2-10% on average.

While hazard data for most of the SIDS endpoints exists for the vast majority of the individual chemicals identified within Solvent C, one can still not deny that it is not known whether the hazards identified for the various endpoints might be affected by their presence as part of a mixture. Exposure to chemicals as part of a mixture can obviously do one of three things to the toxicity of the individual chemicals, increase it, decrease it, or have no effect. In the latter case, an estimate of the hazard potential may simply be based on the relative fractional percentage that each chemical is present at. However, it is believed that the magnitude of any such interactive impact on the toxicity of

the chemicals present in solvent C would be of minimal consequence to the overall toxicity. This conclusion is based on the fact that the toxicity data identified on the individual chemicals (described later in the test plan) indicates that they are of such a low hazard that there exists a wide margin of safety when put in the context of the likely amounts of material humans or the environment may be exposed to. Furthermore, Eastman believes that despite the goals of the HPV program to generate hazard assessment data, the need to conduct further tests still needs to be put into the context of the risk associated with exposure.

There is minimal chance for exposure to Solvent C in the workplace as it is essentially manufactured and handled in closed-systems, and its primary (approximately 93%) use is as a fuel for burning. In this application, product is either shipped by tank truck to other sites within the company where it is burned directly or marketed to a few customers where it is blended into home heating fuel oils at a level well under 1%. Other occasional uses of this product include its use as a solvent in asphalt production and as part of a process solvent in the industrial extraction of phosphoric acid from rock. This latter end-use is performed within closed systems to prevent exposure to the entire processing solvent. Overall, there are a very limited number of customers using Solvent C with the potential for exposure primarily manifested during its transfer to and from tank trucks or under conditions of an industrial accident. Thus, exposures are very limited in both their potential duration (acute) and frequency (intermittent), and would tend to be dermal in nature.

In conclusion, Solvent C is a complex mixture comprised of several chemicals present in varying levels. It is manufactured, handled, and marketed into end uses in such a manner that exposures are very limited and insignificant except under conditions of an accident. While there are no hazard data on Solvent C per se, hazard assessment information are available for most all the endpoints for many of the for the individual chemicals identified in Solvent C. The data on the individual chemicals indicate that they are all of low toxicity. Eastman believes that due to the low hazard potential of these individual chemicals that this information can be used to adequately characterize the hazard potential of Solvent C, especially when put in the context of the anticipated exposure. The goal of the HPV program is to have a screening level of understanding of the hazards presented by a chemical available to the public. Eastman believes the data identified to date that are presently available to the EPA and the general public, in total, fulfill this objective and that further toxicity studies would not be warranted on a chemical mixture whose constituents are of such low toxicity, are present in varying levels, and has such a low potential for human exposure. Accordingly, Eastman believes that the obligations of our commitment to this chemical in the HPV challenge program have been completed through this submission.

Table 1 - Solvent C (CAS No.:68990-21-6) "Typical" Composition and General Comments

CAS No.	Chemical	Composition Percentage[1]	General Comments
10143-60-9	di-2-Ethylhexyl ether	25-35	The only data located on this chemical was an LD_{50} that indicates it is of low toxicity (LD_{50} of 33.9 g/kg; Smyth, H.F., 1954). It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. The EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	Material is an FDA-approved food flavoring agent under 21 CFR 172.515 and is naturally present in many types of fruits. It is fully expected to metabolize to butyric acid and n-butanol in mammals. Both these chemicals are in the ICCA HPV program. Butanol was reviewed at SIAM 13 and butyric acid is scheduled for SIAM 16.
126-30-7	Neopentyl glycol	7-11	An OECD/SIDS assessment has been completed with a conclusion that this substance is presently of low priority for further work.
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	A complete test plan with robust summaries for all end points was submitted into the EPA as part of the HPV program. The test plan was reviewed and a revised test plan was posted September 20, 2002.
71-36-3	n-butyl alcohol	5-10	Material is an FDA-approved food-flavoring agent under 21 CFR 172.515. Material is in the ICCA/SIDS program and was reviewed at SIAM 13.
94-96-2	2-Ethyl-1,3-hexanediol	5-10	The EPA has already reviewed data on this chemical as part of a registration for its use as an insect repellant for humans. Its registration has since been cancelled. The CIR expert panel published a review on its use in cosmetic products. Thus, essentially all SIDS data are available to the public through peer-reviewed journal articles.
NA	Alkyl Acetals	2-10	Formed by a reaction between alcohols and aldehydes. The reaction is readily reversed in the presence of an acid.
104-76-7	2-Ethylhexanol	4-6	An OECD/SIDS assessment was conducted in 1991 (US and Sweden were its sponsors). The CIR expert panel is in the process of publishing a review on its use in cosmetic products.
78-83-1	Isobutyl alcohol	2-6	Material is an FDA-approved food-flavoring agent under 21 CFR 172.515. Material is in the ICCA/SIDS program and is scheduled for SIAM 17.
97-85-8	Isobutyl isobutyrate	2-6	Material is an FDA-approved food-flavoring agent under 21 CFR 172.515. Material is in the ICCA/SIDS program and is scheduled for SIAM 17.
107-92-6	Butyric acid	1-2	Material is an FDA-approved food-flavoring agent under 21 CFR 172.515. Material is in the ICCA/SIDS program and is scheduled for SIAM 16.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.

SIDS DATA SUMMARY

Currently there are no data specifically assessing any of the SIDS endpoints for Solvent C; accordingly, no robust summaries have been prepared on Solvent C. An absence of studies is due to the high degree of variability in the composition of this compound and its primary use and limited exposures. Furthermore, the results of any test conducted on such a material would be anticipated to a low level of reliability and applicability. However, in general, there are significant amounts of data present, either from actual studies or from computer model estimations, for each endpoint from tests conducted on most of the chemicals found within Solvent C. Since much of these data were derived from draft documents not prepared by Eastman, we do not believe these summaries should be included within this assessment. However, these data, and where they are located for the public to peruse, have been briefly summarized to assist in the assessment of each endpoint as it pertains to the potential hazards of Solvent C. The quality of the referenced data is believe to be assured through the fact that five chemicals found in Solvent C will be, or have been, reviewed as part of their participation in various HPV, ICCA and OECD SIDS program. The EPA reviews the data submitted to these programs to ensure they are of high quality and applicability to make a hazard assessment of the various endpoints. In draft form, these studies currently possess Klimisch reliability classifications of 1 or 2 (reliable without restriction or reliable with restrictions, respectively). In addition, it is believed that the FDA has previously reviewed some of their data in support of their use as food additives. One chemical, 2-ethyl-1,3-hexanediol, is not in any HPV program. However, it is present in low amounts (5-10%) and the EPA has previously reviewed data to support its approval for use by humans as an insect repellant. Its data has also been reviewed by an independent panel of experts who reviewed the suitability of the use of this chemical in cosmetic products. The mammalian data used in the EPA's assessment and the review and conclusions by the cosmetic expert panel are currently available to the public in peer-reviewed journals. Thus, these data also believed to be of sufficient quality. An additional chemical not present in any HPV programs is di-2-ethylhexyl ether. Is toxicity potential for some endpoints was estimated by computer modeling programs (DEREK/METEOR v6.0.0). This program assessed it for structural alerts associated with carcinogenicity and mutagenicity and predicted its potential metabolites. Results of this modeling program indicated it to be of low toxicity potential as no structural alerts were identified. Acute toxicity data on this chemical confirms it is relatively harmless with an LD_{50} of almost 34,000 mg/kg. Thus, data are present to support the primary exposure scenarios to Solvent C that are primarily of acute in nature. Eastman believes that further evidence of the low hazard potential likely associated with this chemical is garnered by the fact that is listed the EPA as a Class 3 inert ingredient approved for use in pesticides. Such uses would likely pose significantly more exposures to man or the environment as opposed to its presence in Solvent C. The EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed. If this assessment reveals an unanticipated hazard, Eastman will review these results in context for that hazard to be manifested under the current conditions of its use.

Eastman believes that it is important that when reviewing these data, any concern that may be generated over the presence of a data gap with any particular chemical for some endpoints needs to be put into context with the anticipated exposure to evaluate its significance. The significance of the low exposure potential for Solvent C is also pertinent as it is unknown as to how the toxicity of the chemicals comprising it may change due to their presence as a mixture. However, the fact that exposure is so low, a wide margin of error is created should any toxicity potentiation occur. Thus, it is believed that the hazards of the mixture may be surmised by the potential hazards associated with its constituents as pure chemicals.

I. PHYSICAL CHEMISTRY ENPOINTS

PHYSICAL CHEMICAL ENDPOINTS

There are no data on the physical chemical properties of Solvent C. It would not be practical do any measurements as its composition is of such a variable nature. The below table list the basic physical chemical properties of the major chemicals identified within solvent C. The material is sold as a liquid at ambient temperatures. In general, the components are soluble in water as indicated by low partition coefficients and have relatively low vapor pressures. It is unknown how their presence in a mixture will impact these values. However, the presence of the alcohols would be anticipated to enhance the water solubility of the less polar components, particularly di-2-ethylhexyl ether that has an estimated K_{ow} of 6.8.

Physical Chemical Data[1]

CAS No.	Chemical	Composition Percentage[2]	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mmHg)	Partition Coefficient	Water Solubility (mg/L)
10143-60-9	di-2-Ethylhexyl ether	25-35	18	269	0.0162	6.8	0.04
109-21-7	Butyl butyrate	8-16	-92	166	1.81	2.8	309
126-30-7	Neopentyl glycol	7-11	130	208	0.00249	0.16	82,530
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	52	235	0.00291	1.49	6,879
71-36-3	n-butyl alcohol	5-10	-90	118	6.7	0.84	76,700
94-96-2	2-Ethyl-1,3-hexanediol	5-10	-40	244	0.003	1.6	3,389
NA	Alkyl Acetals	2-10	NA	NA	NA	NA	NA
104-76-7	2-Ethylhexanol	4-6	-70	185	0.136	2.73	1,379
78-83-1	Isobutyl alcohol	2-6	-108	108	10.4	0.77	97,120
97-85-8	Isobutyl isobutyrate	2-6	-81	149	4.33	2.68	412
107-92-6	Butyric acid	1-2	-6	163	1.65	1.07	66,060

1. All data were obtained from estimations or experimental database matches within EPIWIN v3.10.
2. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.

II. ENVIRONMENTAL FATE ENDPOINTS

Photodegradation

There all no data estimating the photodegradation potential and estimated atmospheric half-life of Solvent C as it is a mixture. Such estimations are not feasible as the physical chemical properties of Solvent C vary with its composition and would be anticipated to impact volatility. In general, it is theorized that photodegradation would not be anticipated to be a significant route of removal. This conclusion is based on the low vapor pressures exhibited by many of the constituents and due to their individual fugacity estimates that predict low partition into air. Furthermore, Solvent C is produced and handled in such a manner that releases to the atmosphere would be very limited.

Water Stability

There all no data estimating the water stability of Solvent C as it is a mixture. However, some of the compounds found within it contain ester linkages that may be susceptible to hydrolysis reactions. The rates for such reactions could be estimated on the pure chemical; however, it is unknown how the other chemicals in the mixture will affect these estimates, thus no data are presented for the individual chemicals .

Biodegradation

There are no data estimating the biodegradation potential of Solvent C. Due to the highly variable composition of Solvent C it would be impractical to conduct such a study, as the results would be of uncertain reliability and relevance. Thus, we believe that a basic level of understanding about the potential biodegradability of Solvent C can be obtained through the use of data already generated on its components. Data from actual studies and modeling programs show mixed results as data on some chemicals show an ability to rapidly degrade while others possess a more limited ability. Importantly, releases to the environment are not anticipated except under conditions of an accident during transport as it is produced and handled in essentially closed systems that prevent significant environmental exposures.

Biodegradation Data

CAS No.	Chemical	Composition Percentage[1]	Result	Method	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35	Variable: "Fast" to "Does not biodegrade"	Estimation: BIOWIN v4.00	It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. The EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	Estimated to biodegrade fast	Estimation: BIOWIN v4.00	It is anticipated that the ester linkage will readily be cleaved to form to butanol and butyric acid. Such metabolic reactions have been demonstrated for many short chain alcohol-acid esters.
126-30-7	Neopentyl glycol	7-11	<1.0%; Not readily biodegradable	OECD 301C	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/ Study was conducted under GLP assurances.
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	>99%: Readily biodegradable	OECD 301A	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm
71-36-3	n-butyl alcohol	5-10	36% of ThOD (24h) 44 % of ThOD (23h) BOD_5 45% of ThOD BOD_5 68% of ThOD BOD_5 33% of ThOD BOD_{20} 92% of ThOD BOD_5/COD range of 0.42 to 0.74	Aerobic; un-adapted sludge Aerobic; adapted sludge Aerobic; synthetic sea water Aerobic; fresh water Aerobic; fresh water Aerobic; fresh water; un-adapted sludge.	OECD SIDS assessment for SIAM 13. Gerhold and Malaney, 1966 McKinney and Jeris, 1955 Price *et al.,* 1974 Price *et al.,* 1974 Dore *et al.*, 1974 Union Carbide Corporation, 1992 Lyman *et al.*, 1982
94-96-2	2-Ethyl-1,3-hexanediol	5-10	36% 67% 100%	OECD 303A OECD 301E Zahn-Wellens test; EC 88/302	MSDS; Dixie Chemical Company

NA	Alkyl Acetals	2-10	No data		Material is comprised of several chemicals
104-76-7	2-Ethylhexanol	4-6	BOD_{20} 86% 100%	Aerobic; non-acclimated sludge Zahn-Wellens test	OECD SIDS SIAP and Draft dossier for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/
78-83-1	Isobutyl alcohol	2-6	99 % (5 days) 99 % (14 days) 74 % (28 days)	Directive 84/449/EEC, C.3 OECD Guide-line 301 A OECD Guide-line 301 D	IUCLID document submitted to EPA for SIAM 17.
97-85-8	Isobutyl isobutyrate	2-6	<1.0% Not readily biodegradable	OECD 301B	OECD SIDS Dossier submitted to EPA for SIAM 17
107-92-6	Butyric acid	1-2	72% (5.8 days) 46% after 2 days, 48% after 10 days, 58% after 30 days	Similar to OECD 301C:Modified MITI Test Warburg Respirometer (standard manometric techniques)	OECD SIDS assessment for SIAM 13 Dias, E.F. and M. Alexander. (1971). Effect of Chemical Structure on the Biodegradability of Aliphatic Acids and Alcohols. *Appl. Micro.* 22(6):1114-1118.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.

Fugacity

There are no data estimating the fugacity distribution patterns of Solvent C in the environment. Such estimations are not able to be conducted, as the physical chemical properties of Solvent C will vary with the compositional variability. However, based on the physical chemical properties of its components through the use of fugacity estimations on the individual components (individual fugacity data are not shown), it may be theorized that Solvent C will likely distribute into both soil and water in fairly equal proportions. However, it is unknown how the other chemicals in the mixture will affect these estimates, thus no data are presented for the individual chemicals.

III. ECOTOXICITY ENDPOINTS

There are no data estimating the acute toxicity potential of Solvent C to fish, Daphnia or other invertebrates, or algae. Due to the highly variable composition of Solvent C it would be impractical to conduct such a study, as the results would be of uncertain reliability and relevance. Thus, we believe that a basic level of understanding about its potential toxicity to these organisms can be obtained through the use of data already generated on the components. Data from studies conducted on many of the chemicals found within Solvent C indicate a low potential for toxicity to all these species. The results from the ECOSAR modeling program for the toxicity of butyl butyrate and actual data on isobutyl butyrate, suggest they may be more toxic. The significance of these low estimates is somewhat tempered by their overall low percentage levels within Solvent C. Due to a K_{ow} estimate of 6.80 for di-2-ethylhexyl ether, estimation results for acute toxicity effects to all three species were not obtainable. Importantly, releases to the environment are not anticipated except under conditions of an accident during transport as it is manufactured and handled in essentially closed systems that prevent significant environmental exposures. In addition, environmental exposures are limited by the fractional presence of each component.

Fish Toxicity Data

CAS No.	Chemical	Composition Percentage[1]	LC_{50} NOAEL[2] ppm	Method	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35		No Data	The estimated K_{ow} of 6.8 precludes use of ECOSAR modeling program for fish. It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. Such uses would obviously have significant environmental releases. Thus, it is assumed by Eastman that the EPA does not believe it poses a significant environmental threat. EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	7.9	Estimation	EPIWIN: ECOSAR
126-30-7	Neopentyl glycol	7-11	>1,000	OECD	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	>700	Other	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm
71-36-3	n-butyl alcohol	5-10	1,000 – 1,900 (24 hr) 1,200 – 1770 (48 hr) 1,400 – 1,940 (96 hr)	Other	OECD SIDS assessment for SIAM 13. Multiple studies were listed with multiple species and the values listed represent the ranges.
94-96-2	2-Ethyl-1,3-hexanediol	5-10	>1,000 (48 hr)	Other: DIN 38412	MSDS; Dixie Chemical Company
NA	Alkyl Acetals	2-10			Material is comprised of several chemicals
104-76-7	2-Ethylhexanol	4-6	27- 29.5 (24 hr) 96 – 144 (48 hr)	Other: material was in water; second study it was in the feed	OECD SIDS SIAP and Draft dossier for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/
78-83-1	Isobutyl alcohol	2-6	2,600 – 4,300 (24 hr) 1,520 - >2,000 (48 h) 375 - >5,013 (96 hr)		IUCLID document submitted to EPA for SIAM 17. Multiple studies were listed with multiple species and the values listed represent the ranges.
97-85-8	Isobutyl isobutyrate	2-6	13.4 (96 hr)	OECD 203	Chemical is to be submitted to the EPA for inclusion in SIAM 17. Study was conducted under GLP assurances.

107-92-6	Butyric acid	1-2	90 (freshwater) 230 (sea water) (both 48 hr)	Other	OECD SIDS assessment for submitted to EPA for SIAM 16.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.
2. All studies or estimation values, unless noted, are for 96 hours in duration

Daphnia Toxicity Data

CAS No.	Chemical	Composition Percentage[1]	EC_{50} NOAEL[2] ppm	Method	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35		No Data	The estimated K_{ow} of 6.8 precludes use of ECOSAR modeling program for daphnia. It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. Such uses would obviously have significant environmental releases. Thus, it is assumed by Eastman that the EPA does not believe it poses a significant environmental threat. EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	20.1	Estimation	EPIWIN: ECOSAR
126-30-7	Neopentyl glycol	7-11	>1,000	OECD	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	>109	OECD 202	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm Study was conducted under GLP assurances.
71-36-3	n-butyl alcohol	5-10	1,880 – 2,337 (24 hr) 1,983 (48 hr)	Other	OECD SIDS assessment for SIAM 13. Multiple studies were listed and the values listed represent the ranges.
94-96-2	2-Ethyl-1,3-hexanediol	5-10	811 (24 hr)	Other: DIN 38412	MSDS; Dixie Chemical Company
NA	Alkyl Acetals	2-10			Material is comprised of several chemicals
104-76-7	2-Ethylhexanol	4-6	26 – 44 (24 hr) 35 (48 hr) 31 –176 (? Hr)	Other	OECD SIDS SIAP and Draft dossier for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/

78-83-1	Isobutyl alcohol	2-6	1,000 – 1463 (24 hr) 600 – 1,439 (48 hr) 949 (96 hr)	Other	IUCLID document submitted to EPA for SIAM 17. Multiple studies were listed with multiple species and the values listed represent the ranges.
97-85-8	Isobutyl isobutyrate	2-6	57.6	OECD 202	Chemical is to be submitted to the EPA for inclusion in SIAM 17. Study was conducted under GLP assurances.
107-92-6	Butyric acid	1-2	1950 (24 hr)	Other: DIN 38412	OECD SIDS assessment for submitted to EPA for SIAM 16.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.
2. All studies or estimation values, unless noted, are for 48 hours in duration

Algal Toxicity Data

CAS No.	Chemical	Composition Percentage[1]	EC_{50} NOAEL[2] ppm	Method	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35		No Data	The estimated K_{ow} of 6.8 precludes use of ECOSAR modeling program for algae. It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. Such uses would obviously have significant environmental releases. Thus, it is assumed by Eastman that the EPA does not believe it poses a significant environmental threat. EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	0.65	Estimation	EPIWIN: ECOSAR
126-30-7	Neopentyl glycol	7-11	>1,000 (72 hr)	OECD	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	>110	OECD 201	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm Study was conducted under GLP assurances.
71-36-3	n-butyl alcohol	5-10	>500 100 – 875 (8 days)	Other	OECD SIDS assessment for SIAM 13. Multiple studies and species were listed and the values listed represent the ranges.
94-96-2	2-Ethyl-1,3-hexanediol	5-10	164	Estimation	EPIWIN: ECOSAR
NA	Alkyl Acetals	2-10			Material is comprised of several chemicals

104-76-7	2-Ethylhexanol	4-6	10 – 50 (48 hr)	Other	OECD SIDS SIAP and Draft dossier for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/
78-83-1	Isobutyl alcohol	2-6	6,400 (24 hr) 1,250 (48 hr) 350 (8 day)	Other	IUCLID document submitted to EPA for SIAM 17. Multiple species were assessed at different time points..
97-85-8	Isobutyl isobutyrate	2-6	0.77	Estimation	EPIWIN: ECOSAR
107-92-6	Butyric acid	1-2	318 - 2,600 (8 day)	Other	OECD SIDS assessment for submitted to EPA for SIAM 16. Value in draft dossier was listed to be an EC3.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.
2. All studies or estimation values, unless noted, are for 96 hours in duration

IV. MAMMALIAN TOXICITY ENDPOINTS

There are no data estimating the toxicity potential of Solvent C for any of the mammalian endpoints. However, as can be seen in the below tables, data do exist for most of the individual chemicals identified within it. Eastman believes that concerns that may be raised over the potential for toxicity potentiation from their presence in a mixture is negated by the large margins of exposure that exist for Solvent C. The data utilized were derived from studies whose data quality reliability codes range from a 1 (Reliable without restriction) to a 2 (Reliable with restriction). Thus, all data should be deemed of being of suitable quality to support an assessment of the potential acute toxicity of Solvent C. Summaries from many of these studies are currently available to the public, or will be made available in the future, at the indicated references.

ACUTE TOXICTY

As can be seen in the below table, acute oral toxicity data in rodents exist for most all the chemicals that comprise Solvent C. Results of the various studies indicate the materials are all of very low toxicity ranging from slightly toxic (LD_{50} 0.5 – 5g/kg) to practically non-toxic (LD_{50} 5-15 g/kg) and even relatively harmless (LD_{50} >15 g/kg). The impact on their toxicity potential due to their presence in a mixture is unknown. However, when these data are put into context of the anticipated low exposures, there is a wide margin of safety should there be any enhancement. Thus, Eastman believes there would be little value in conducting a new study on Solvent C to assess its acute toxicity.

Acute Toxicity Data

CAS No.	Chemical	Composition Percentage[1]	Oral LD_{50}	Reference
10143-60-9	di-2-Ethylhexyl ether	25-35	33,900 mg/kg (rat)	Smyth, H.F. *AMA Arch. Ind. Hyg. Occup. Med.* 10, 61-68 (1954)
109-21-7	Butyl butyrate	8-16	9,500 mg/kg (rabbit)	Munch, J.C.*Ind. Med. Surg*. 41(4):31 (1972) from Butyl n-butyrate: Fragrance raw materials monographs. *Food Cosmetics Toxicology* **17**, 521-522 (1979)
126-30-7	Neopentyl glycol	7-11	3,200 mg/kg (rat)	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	800 - 1,600 mg/kg (rat) 1,600 - 3,200 mg/kg (mouse)	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm

71-36-3	n-butyl alcohol	5-10	790 - 4,360 mg/kg (rat) 2,680 mg/kg (mouse)	OECD SIDS assessment for SIAM 13
94-96-2	2-Ethyl-1,3-hexanediol	5-10	2.6 - 9.85 ml/kg (rat)	Final report by the Cosmetics Ingredients Review Expert Panel: *J. Amer. Coll. Toxicol.* 13(6):418-436 (1994)
NA	Alkyl Acetals	2-10		
104-76-7	2-Ethylhexanol	4-6	600 - >3,000 mg/kg (various species)	OECD SIDS SIAP from SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/
78-83-1	Isobutyl alcohol	2-6	2,460 – 3,350 mg/kg (rat) 3,500 mg/kg (mouse)	IUCLID document submitted to EPA for SIAM 17.
97-85-8	Isobutyl isobutyrate	2-6	>6,400 mg/kg (rat and mouse)	OECD SIDS Dossier submitted to EPA for SIAM 17.
107-92-6	Butyric acid	1-2	2,940 – 8,790 (rat)	OECD SIDS Dossier submitted to EPA for SIAM 16.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.

REPEAT DOSE TOXICTY

As can be seen in the below table, repeat exposure toxicity data in rodents or approved food intake level assessments exist for many of the chemicals that comprise Solvent C. These chemicals comprise at least 2/3 of its composition on a percentage basis. Results of the various studies indicate the materials are all of low toxicity with the NOAEL levels greater than 100 mg/kg. While do data are available on butyl butyrate, an acceptable daily intake (ADI) of 1 mg/kg has been established by a European Regulatory for its use in foods. The impact on the toxicity potential of these chemicals due to their presence within a mixture is unknown. However, based on the fact that all the materials are of a low toxicity and the level and likelihood of repeated exposure is low, a wide margin of safety exists should any one chemical potentiate the toxicity of another chemical. Currently there are no data available for one of the chemicals in this mixture, di-2-ethylhexyl ether. This chemical may be present at up to 35% of the mixture. Importantly, this chemical has a very large LD_{50} value (33,900 mg/kg) that would allow for the application of a 100 or 1,000 fold uncertainty factor to make up for an absence of repeated exposure data. In addition, the results of a predictive biotransformation-modeling program (DEREK/METEOR v6.0.0) indicate the material would likely be metabolized through simple oxidation reactions on its side chains followed by phase II conjugation and excretion. Such reactions would be anticipated to result in a detoxification of this molecule. It was noted that a possible metabolic route could lead to the formation of 2-EH. However, this route would involve the cleavage of an ether linkage and would be believed to be minor. Data is available for 2-EH as it is one of the chemicals identified in Solvent C. Since the EPA list this chemical as an inert ingredient for use in pesticide formulations, Eastman believes the EPA does not have a high level of concern over its potential toxicity. Overall, when these data are put into context of the anticipated low and infrequent exposures, Eastman believes there would be little value in conducting a new study on Solvent C to assess its toxicity following repeated exposures.

Repeat Dose Toxicity Data

CAS No.	Chemical	Composition Percentage[1]	NOAEL	Method	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35	No data found		It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. The EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	No data found		The Council of Europe established an acceptable daily intake (ADI) of 1 mg/kg for use in foods [Fragrance raw materials monographs. *Food Cosmetics Toxicology* **17**, 521-522 (1979)]. It is anticipated that the ester linkage will readily be cleaved to form to butanol and butyric acid. Such metabolic reactions have been demonstrated for many short chain alcohol-acid esters (e.g. isobutyl isobutyrate).
126-30-7	Neopentyl glycol	7-11	100 mg/kg	OECD 422; gavage	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/ Study was conducted under GLP assurances.
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	0.5%	Other: 60 days; dietary	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm
71-36-3	n-butyl alcohol	5-10	125 mg/kg	Other: 13 week; gavage	OECD SIDS assessment for SIAM 13. Study was conducted under GLP assurances.
94-96-2	2-Ethyl-1,3-hexanediol	5-10	480 mg/kg	Other: 13 week; oral	Smyth et al. (1951). Range-Finding Toxicity Data: List IV. *AMA Arch. Ind. Hyg. Occup. Med.* 4:119-22. Reported in the final report by the Cosmetics Ingredients Review Expert Panel: *J. Amer. Coll. Toxicol*. 13(6):418-436 (1994) VanMiller, J.P., *et al.* (1995). Repeated Exposure Toxicity of 2-Ethyl-1,3-Hexanediol by Cutaneous Applications to the Rat for 9 and 90 Days. *Vet. Hum. Toxicol.* **37(1)**, 33-36.
			3,768 mg/kg (males) 1,884 mg/kg (females)	Other: 13 week; dermal	
NA	Alkyl Acetals	2-10		No data	Material is comprised of several chemicals
104-76-7	2-Ethylhexanol	4-6	125 mg/kg	Other: 13 week; oral	OECD SIDS SIAP for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/
78-83-1	Isobutyl alcohol	2-6	16,000 ppm (1,450 mg/kg)	OECD 408; 90 days Drinking water	IUCLID document submitted to EPA for SIAM 17. Study was conducted under GLP assurances.
97-85-8	Isobutyl isobutyrate	2-6	1000 mg/kg	Other: gavage 18 weeks	OECD SIDS Dossier submitted to EPA for SIAM 17. Drake et al. (1978). Short-Term Toxicity Study of Isobutyl Isobutyrate in Rats. Food Cosmetics Toxicology, 16:337-342.

107-92-6	Butyric acid	1-2	125 mg/kg	Other: 13 week; gavage	OECD SIDS assessment for SIAM 13 and OECD SIDS Dossier submitted to EPA for SIAM 16. Test material was n-butanol that has been shown to be rapidly metabolized to butyric acid.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.

GENOTOXICITY

As can be seen in the below table data assessing both mutagenicity and chromosomal aberration potential were identified on the chemicals comprising Solvent C. Results from all studies indicate they are not genotoxic. Currently there are no data available for one of the chemicals in this mixture, di-2-ethylhexyl ether. However, the results of a predictive biotransformation-modeling program (DEREK/METEOR v6.0.0) indicate the material would likely be metabolized through simple oxidation reactions on its side chains followed by phase II conjugation and excretion, and no mutagenic alerts were identified by this program. Thus, the potential for Solvent C to be genotoxic is believed to be low.

Genotoxicity Data

CAS No.	Chemical	Composition Percentage[1]	Mutation	Aberrations	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35	No Data	No Data	It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. The EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed. Metabolism modeling did not predict the formation of any mutagenic metabolites.
109-21-7	Butyl butyrate	8-16	See n-butanol and butyric acid	See n-butanol and butyric acid	It is anticipated that the material would be metabolized to butanol and butyric acid. Both of which are not genotoxic.
126-30-7	Neopentyl glycol	7-11	Negative	Negative	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/ Studies were conducted under GLP assurances.
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	Negative	Negative	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm Studies were conducted under GLP assurances.
71-36-3	n-butyl alcohol	5-10	Negative	Negative	OECD SIDS assessment for SIAM 13.
94-96-2	2-Ethyl-1,3-hexanediol	5-10	Negative	Negative	Slesinski, R.S., *et al.*, (1988). In Vitro and In Vivo Evaluation of the Genotoxic Potential of 2-Ethyl-1,3-Hexanediol. *Toxicology*, **53(2-3),** 179-198. Reported in the final report by the Cosmetics Ingredients Review Expert Panel: *J. Amer. Coll. Toxicol*. 13(6):418-436 (1994)
NA	Alkyl Acetals	2-10	No Data	No Data	Material is comprised of several chemicals
104-76-7	2-Ethylhexanol	4-6	Negative	Negative	OECD SIDS SIAP for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/

78-83-1	Isobutyl alcohol	2-6	Negative	Negative	IUCLID document submitted to EPA for SIAM 17. Studies were conducted under GLP assurances.
97-85-8	Isobutyl isobutyrate	2-6	Negative	Negative	OECD SIDS Dossier submitted to EPA for SIAM 17. OECD SIDS Dossier being drafted for isobutyric acid (will be submitted to EPA for presentation in a future SIAM. It is anticipated that this chemical will be metabolized to isobutanol and isobutyric acid. Isobutanol is metabolized to isobutyric acid.
107-92-6	Butyric acid	1-2	Negative	Negative	OECD SIDS Dossier submitted to EPA for SIAM 16

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

As can be seen in the below tables, data assessing reproductive and developmental toxicity potential exist for most all the chemicals that comprise Solvent C. Results of the various studies indicate the materials are all of low potential to induce reproductive or developmental toxicity. The impact on their toxicity potential subsequent to an exposure as a mixture is unknown. However, based on the fact that all the materials are of a low toxicity, a wide margin of safety exists should any one chemical potentiate the toxicity of another one. Currently there are no data available for one of the chemicals in this mixture, di-2-ethylhexyl ether. This chemical may be present at up to 35% of the mixture. The results of a predictive biotransformation-modeling program (DEREK/METEOR v6.0.0) indicate the material would likely be metabolized through simple oxidation reactions on its side chains followed by phase II conjugation and excretion. Such reactions would be anticipated to result in a detoxification of this molecule. No structural alerts were identified for mutagenicity, which could be a mechanism of inducing teratogenic effects. It was noted that a possible metabolic route could lead to the formation of 2-EH. However, this route would involve the cleavage of an ether linkage and would be believed to be minor. Data is available for 2-EH as it is one of the chemicals comprising Solvent C. Since the EPA list this chemical as an inert ingredient for use in pesticide formulations, Eastman believes the EPA does not have a high level of concern over its potential developmental or reproductive toxicity. Overall, when these data are put into context of the anticipated low and infrequent exposures, Eastman believes there would be little value in conducting a new study on Solvent C to assess its potential to impact reproduction.

Developmental Toxicity Data

CAS No.	Chemical	Composition Percentage[1]	NOAEL	Method[2]	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35	No data found		It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. The EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	See n-butanol		The Council of Europe established an acceptable daily intake (ADI) of 1 mg/kg for use in foods [Fragrance raw materials monographs. *Food Cosmetics Toxicology* **17**, 521-522 (1979)]. It is anticipated that this material will metabolized to butanol and butyric acid. Such a reaction has been definitively demonstrated for many short chain alcohol acid compounds linked by an ester linkage.
126-30-7	Neopentyl glycol	7-11	1,000 mg/kg	OECD 422; gavage	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/ Study was conducted under GLP assurances.

144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	1.0%	Other: 3 generation; dietary	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm
71-36-3	n-butyl alcohol	5-10	6,000 ppm	Other: Days 1-20; inhalation	OECD SIDS assessment for SIAM 13: Nelson, B.K., et al. (1989). Behavioral Teratology investigation of 1-Butanol in Rats. *Neurotoxicology and Teratology*. 11(3):313-315. Nelson, B.K.., et al. (1989). Lack of selective developmental toxicity of three butanol isomers administered by inhalation to rats. *Fund. and App. Toxicol.* 12(3):469-479.
			3,500 ppm	Other: Days 1-19; inhalation	
94-96-2	2-Ethyl-1,3-hexanediol	5-10	1,000 mg/kg	Other: Days 6-15; gavage	Developmental toxicity probe study; Unpublished Kodak data Reported in the final report by the Cosmetics Ingredients Review Expert Panel: *J. Amer. Coll. Toxicol*. 13(6):418-436 (1994) Neeper-Bradley, T.L., et al. (1994) Evaluation of the developmental toxicity potential of 2-ethyl-1,3-hexanediol in the rat by cutaneous application *J. Toxicol.-Cut & Ocular Toxicol.* 13(3):203-214.
			1 ml/kg	Other: Days 6-15; dermal	
NA	Alkyl Acetals	2-10		No data	Material is comprised of several chemicals
104-76-7	2-Ethylhexanol	4-6	(o) 130 mg/kg - rat (o) 191 g/kg -mouse (d) 840 mg/kg (i) <0.85 mg/l	Other: oral (rat and mouse), dermal, and inhalation	OECD SIDS SIAP for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/
78-83-1	Isobutyl alcohol	2-6	10 mg/L (both species)	OECD 414; inhalation; rat and rabbit	IUCLID document submitted to EPA for SIAM 17. Study was conducted under GLP assurances.
97-85-8	Isobutyl isobutyrate	2-6	See isobutanol data		OECD SIDS Dossier submitted to EPA for SIAM 17. This material has been demonstrated to be rapidly metabolized to isobutanol and butyric acid.
107-92-6	Butyric acid	1-2	See n-butanol data		OECD SIDS Dossier submitted to EPA for SIAM 16. See n-butanol data as n-butanol is metabolized to butyric acid.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.
2. Except where noted, all studies were conducted in rats.

Reproductive Toxicity Data

CAS No.	Chemical	Composition Percentage[1]	NOAEL	Method	Comments / Reference
10143-60-9	di-2-Ethylhexyl ether	25-35	No data found		It is listed by the EPA as a Class 3 inert ingredient for use in pesticide formulations. The EPA is in the process of preparing toxicological and ecological assessments for this class level of inert ingredients. Such assessments will be available for the public to review when completed.
109-21-7	Butyl butyrate	8-16	See n-butanol		The Council of Europe established an acceptable daily intake (ADI) of 1 mg/kg for use in foods [Fragrance raw materials monographs. *Food Cosmetics Toxicology* **17**, 521-522 (1979)]. It is anticipated that this material will metabolized to butanol and butyric acid. Such a reaction has been definitively demonstrated for many short chain alcohol acid compounds linked by an ester linkage.
126-30-7	Neopentyl glycol	7-11	1,000 mg/kg	OECD 422; gavage	OECD SIDS Dossier: http://cs3-hq.oecd.org/scripts/hpv/ Study was conducted under GLP assurances.
144-19-4	2,2,4-Trimethyl-1,3-pentanediol	7-11	1.0%	Other: 3 generation; dietary	US-HPV challenge program: http://www.epa.gov/opptintr/chemrtk/volchall.htm
71-36-3	n-butyl alcohol	5-10	<300 mg/kg (LOEL)	Other: 13 week; oral	OECD SIDS SIAR for SIAM 13: Krystyna Sitarek, Bogumila Berlinska and B. Baranski (1994).“Assessment of the Effect of N-Butanol Given to Female Rats in Drinking Water on Fertility and Prenatal Development of Their Offspring”. *International Journal of Occupational Medicine and Environmental Health*, Vol. 7, No. 4, pp. 365-370. The second study listed exposed animals to butyl acetate, which is cleaved to yield butanol.
			3,000 ppm	Other: 14 week; inhalation	
94-96-2	2-Ethyl-1,3-hexanediol	5-10	3,768 mg/kg (males) 1,884 mg/kg (females)	Other: 13 week; dermal	VanMiller, J.P., *et al.* (1995). Repeated Exposure Toxicity of 2-Ethyl-1,3-Hexanediol by Cutaneous Applications to the Rat for 9 and 90 Days. *Vet. Hum. Toxicol.* **37(1)**, 33-36.
NA	Alkyl Acetals	2-10	No data		Material is comprised of several chemicals
104-76-7	2-Ethylhexanol	4-6	125 mg/kg	Other: 13 week; oral	OECD SIDS SIAP for SIAM 3 http://cs3-hq.oecd.org/scripts/hpv/

78-83-1	Isobutyl alcohol	2-6	0.77 mg/L (NOEL)	Other; 90 days; inhalation	IUCLID document submitted to EPA for SIAM 17. Changes in some stages of sperm maturation were noted at higher doses. The biological significance of this change was uncertain.
97-85-8	Isobutyl isobutyrate	2-6	See isobutanol data		OECD SIDS Dossier submitted to EPA for SIAM 17. This material has been demonstrated to be rapidly metabolized to isobutanol and butyric acid.
107-92-6	Butyric acid	1-2	See n-butanol data		OECD SIDS Dossier submitted to EPA for SIAM 16. See n-butanol data as n-butanol is metabolized to butyric acid.

1. The percentages listed represent the typical ranges a specific component may be found if present. Such that the actual ranges really begin at 0%.